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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/891,943	06/26/2001	W. Michael Gallatin	27866/37524	2656

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/891,943	GALLATIN ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

REFERENCES NOT PROVIDED

1) ☒ Notice of References Cited (PTO-892) CITED BY APPLICANT

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .

4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment, filed 8/14/03, has been entered.
Claims 11, 12 and 14 have been amended.

Claims 11-14 are pending.

Claims 1-10 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's amendment, filed 8/14/03.
The rejections of record can be found in previous Office Action, mailed 2/11/03.

3. The filing date of the instant claims is deemed to be the filing date of parent application USSN 08/943,363, filed 10/3/97. It is noted that previous priority applications USSNs 08/605,672; 08/362,652; 08/2886,889; and 08/173,497 do not appear to provide for methods of modulating TNFα release from splenic phagocytes with alphaD-specific antibodies as well as the 205C/205E alphaD-specific antibodies. If applicant desires priority prior to 1/1/91; applicant is invited to point out and provide documentary support for the priority of the instant claims. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

It is noted that applicant's amendment, filed 8/14/03, has updated the status of the priority documents, but still maintains a claim for priority back to USSN 08/173,497, filed 12/23/93.

4. Applicant's amendment, filed 8/14/03, indicates that formal drawings have been submitted, however no such drawings appear for the scanned application.

Given the changes to Image File Wrapper at the USPTO, the examiner does not request another submission of drawings at this time. Such requirements that would be in compliance with 37 CFR 1.84 as set forth in the form PTO-948, mailed 2/11/03, will be considered and addressed if this application is placed in condition for allowance.

The examiner apologizes for any inconvenience to applicant in this matter.

5. Applicant's amendment, filed 8/14/03 has obviated the previous rejection for claim 14 under 35 U.S.C. 112, first paragraph, enablement for the deposit of biological materials.

6. Claims 11-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "alphaD specificity encoded by the amino acid sequence SEQ ID NO: 2 or the nucleic acid sequence SEQ ID NO: 1 " disclosed in the specification and now claimed (and priority applications) as-filed, does not reasonably provide enablement for any "alphaD specificity", including "a polynucleotide that hybridizes to the complement of the polynucleotide of (a) or (b), under conditions that include a final wash in 1X SSC/0.1% SDS at 65° C." to be the specificity targeted in the claimed methods to modulate TNFα release from macrophages or phagocytes in order to inhibit immune responses for the reasons of record.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims. molecule.

Applicant's amendment, filed 8/14/03, have been fully considered but are not found convincing essentially for the reasons of record.

In the absence of functional properties in the context of the recitation of "a polynucleotide that hybridizes to the complement of the polynucleotide of (a) or (b), under conditions that include a final wash in 1X SSC/0.1% SDS at 65° C." set forth in claim 11(c), there are insufficient characteristics that would enable the claimed "alphaD" specificity. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any "alphaD" hybridizing nucleic acid specificity.

While applicant is relying upon the disclosure of certain biological activities of a limited representative number of species to support an entire genus, the recitation of any hybridizing nucleic acid does not provide sufficient predictability and structural constraints to the claimed "alphaD" specificity. The instant invention encompasses targeting any "alphaD" to modulate TNFα release from macrophages or phagocytes in order to inhibit immune responses, yet the instant specification does not provide sufficient guidance and direction how to make and use any hybridizing nucleic acid in the absence of testable functional attributes, as currently encompassed by the claims. For example, the specification does not provide for the correlation between the chemical structure and the function of the genus of "alphaD molecules", currently encompassed by the claimed invention. The reliance on the disclosed limited examples of certain known sequences that encode "alphaD" indicated above and disclosed in the specification as filed does not provide sufficient enablement of any protein encoded by protein encoded by "alphaD molecule encoding hybridizing nucleic acids", as currently claimed. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biology, expression and activities.

Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. ligand or receptor; integrin) requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain binding or functional aspects ligands and receptors and finally what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Because of the lack of sufficient guidance and predictability in determining which structures would lead to "alphaD " encoding nucleic acids other than those disclosed in the specification as filed with the desired properties and that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of proteins encoded by "alphaD" encoding hybridizing nucleic acids targeted by the claimed methods to modulate TNFα release from macrophages or phagocytes in order to inhibit immune responses.

Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

In the absence of sufficient guidance and direction to the structural and functional analysis, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue to make and use proteins encoded by "alphaD" hybridizing nucleic acids other than those disclosed in the specification as filed and now claimed as the target specificity in the claimed methods OR adding testable functional properties associated with the recitation of "a polynucleotide that hybridizes to the complement of the polynucleotide of (a) or (b), under conditions that include a final wash in 1X SSC/0.1% SDS at 65° C." set forth in claim 11(c).

Without sufficient guidance, making and using proteins encoded by "alphaD" hybridizing nucleic acids other than the such proteins encoded by "alphaD" hybridizing nucleic acids recited in the context of testable functional attributes disclosed in the specification as filed as the target specificity in the claimed methods would have been unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Applicant is invited to amend the claims to recite testable functional attributes with respect to claim 11(c). Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06. In addition, applicant is invited to indicate the date of priority for such language.

7. Claims 11-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention

A) Claims 11-14 are indefinite in its recitation of "modulating" because it is ambiguous as to the direction (positive or negative) or degree of said modulating.
Applicant should amend the claims to recite clear positive endpoints.

Applicant's arguments, filed 8/14/03, have been fully considered but are not found convincing essentially for the reasons of record.
Applicant argues that page 19, line 8 of the instant specification defines "modulating" as either the inhibition or enhancement of a particular activity.

However, such endpoints are clearly opposite endpoints and would be inconsistent with one another, Further, this is confusing, given the same method steps and the same ingredients, yet opposite endpoints.

In addition, there is insufficient direction or guidance in the specification as filed for enhancing TNF-α release with anti-αD antibodies. If applicant maintains this position, then a rejection under 35 USC 112, first paragraph, enablement would appear to be appropriate.

B) Applicant's amendment, filed 8/14/03 has obviated the previous rejection of claim 14 with respect to the recitation of "205C" and "205E".

C) Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

8. Claim 11-14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Gallatin et al. (U.S. Patent No. 5,437,958) (see entire document) for the reasons of record.

Applicant's arguments, filed 8/14/03, have been fully considered but are not found convincing essentially for the reasons of record.

Although applicant acknowledges that Gallatin discloses the use of anti-αD antibodies for treating immune or inflammatory responses, Gallatin does not give any particular examples nor suggest modulating TNF-α release. Applicant provides Feliciani et al. (Int. J. Immunpathol. Pharmacol. 12: 55-61, 1999), Takashi et al. (Ann. Allergy Asthma Immunol. 50: 150-155, 2000) and Huang et al. (J. Exp. Med. 193: 713-725, 2001) to indicate that not all inflammatory conditions are associated with TNF-α release.

In contrast to applicant's assertions, Gallatin et al. teach methods of treating immune or inflammatory responses with antibodies that bind alphaD (see Background of the Invention, including column 3, paragraph 2; Brief Description of the Invention; Detailed Description of the Invention). Gallatin et al. Provides further guidance that the nature of the inflammatory conditions associated with macrophages include atherosclerosis, multiple sclerosis and diabetes (column 5, paragraph 5), which are consistent with the instant disclosure (pages 14-15, overlapping paragraph and page 16, paragraph 1).

The claimed functional limitations of modulating TNFα release from macrophages or phagocytes with alphaD-specific antibodies, including the αD I-domain specificity, would be inherent properties of the referenced methods to treat immune or inflammatory responses with inhibitory alphaD-specific antibodies.

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

Even though the claims are drawn to a mechanism by which the alphaD-specific antibodies inhibit immune or inflammatory responses, the claimed methods do not appear to distinguish the prior art teaching the same or nearly the same methods to achieve the same end result. The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Applicant's arguments are not found persuasive.

9. Claims 11-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
claims 1-10 of U.S. Patent No. 6,251,395 and
claims 1-9 of U.S. Patent No. 6,432,404 for the reasons of record.

Applicant's arguments, filed 8/14/03, have been fully considered but are not found convincing essentially for the reasons of record.

Although applicant acknowledges that the patent claims recite methods for inhibiting macrophage infiltration or locomoter injury in the CNS using antibodies to alphaD, applicant asserts in conjunction with Flugel et al. (Eur. J. Immunol 31: 11-22, 2001 and Huang et al. (J. Exp. Med 193: 713-726, 2001) that the administration of anti-alphaD antibodies could inhibit macrophage infiltration into the brain by a number of mechanisms.

Given that the patented claims are drawn to achieving the same or nearly the same endpoints of inhibiting macrophage infiltration, including the 217L and 226H antibody specificities, such patented claims would anticipate the instant methods of inhibiting the same or nearly same macrophage populations. The present claimed functional limitations of modulating TNFα release from macrophages or phagocytes with alphaD-specific antibodies would be inherent properties of the patented methods to inhibit locomoter damage following spinal cord injury or inhibiting inflammation at the site of a central nervous system injury with alphaD-specific antibodies.

Applicant's arguments are not found persuasive.

10 No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
October 30, 2003